

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference T10F1425	FOR FURTHER ACTION	See item 4 below
International application No. PCT/JP2004/017998	International filing date (<i>day/month/year</i>) 26 November 2004 (26.11.2004)	Priority date (<i>day/month/year</i>) 27 November 2003 (27.11.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant TAKASAGO INTERNATIONAL CORPORATION		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input checked="" type="checkbox"/> | Box No. II | Priority |
| <input type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Date of issuance of this report 29 May 2006 (29.05.2006)
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PATENT COOPERATION TREATY

REC'D 06 MAY 2005

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From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

a/b

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/JP2004/017998

International filing date (day/month/year)
26.11.2004

Priority date (day/month/year)
27.11.2003

International Patent Classification (IPC) or both national classification and IPC
C07C51/36, C07C59/64

Applicant
TAKASAGO INTERNATIONAL CORPORATION

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/JP2004/017998

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/JP2004/017998

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-18
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	1-18
Industrial applicability (IA)	Yes: Claims	1-18
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

1) Reference is made to the following documents:

- D1:** MATS T. LINDENBERG ET AL.: "Claisen condensation as a facile route to an alpha-alkoxy-cinnamate: Synthesis of ethyl (2S)-2-ethoxy-3-(4-hydroxyphenyl)propanoate" ORGANIC PROCESS RESEARCH & DEVELOPMENT, vol. 8, no. 6, 21 October 2004 (2004-10-21), pages 838-845, XP002325851
- D2:** EP-A-0 408 338 (TAKASAGO INTERNATIONAL CORPORATION) 16 January 1991 (1991-01-16)
- D3:** US-A-5 783 738 (MATHEY ET AL) 21 July 1998 (1998-07-21)
- D4:** US-A-5 334 758 (SABURI ET AL) 2 August 1994 (1994-08-02)

2) The present application relates to processes for the production of optically active 3-(4-hydroxyphenyl)propionic acids of formula (6) (cf. Claim 1) or carboxylic acids of the broader formula (12) (cf. Claim 7). The processes involve the asymmetric hydrogenation of the corresponding α,β -unsaturated carboxylic acid.

3) Re Item II and VI

The priority document pertaining to the present application was not available at the time of establishing this written opinion. Hence, this is based on the assumption that all claims enjoy priority rights from the filing date of the priority document (27.11.2003). If it later turns out that this is not correct, the document **D1** (published before the filing date of the present application) could become relevant to assess whether the claims satisfy the criteria set forth in Article 33(1) PCT.

4) Re Item V

4.1 Novelty (Art. 33(2) PCT)

D2-D4 disclose (cf. **D2**: examples 1-10; **D3**: examples 5 and 6; and **D4**: examples 18-25) the preparation of 2-acylamino-3-aryl propionic acid. The subject-matter of Claim 7, which appears to be the broadest claim, differs from **D2-D4** in that the substituent on position 2 of the acid is oxygenated and not nitrogenated. The claimed subject-matter is therefore novel.

4.2 Inventive Step (Art. 33(3) PCT)

The documents **D2-D4** are regarded as the closest state of the art for all the independent claims (i.e. claims 1, 2, 3, 7, and 14-18). The difference between the claimed processes and **D2-D4** lies in the substituent on position 2 of the carboxylic acid, which is alkoxy instead of acylamino. The problem to be solved may thus be regarded as providing **alternative** processes for providing optically active propionic acid derivatives.

It is obvious for the skilled person in the art that the asymmetric hydrogenations of **D2-D4** are also applicable to carboxylic acids wherein the α -substituent is an alkoxy. The subject-matter of claims 7 and 14-17 may thus not be regarded as inventive. Claims 1, 2, and 18 further indicate the steps for the preparation of the cinnamic acid which is to be hydrogenated. These steps, however, correspond to trivial reactions, which are well-known in the preparation of α,β -unsaturated carboxylic acids such as cinnamic acid (e.g. Claisen condensation with benzaldehyde) and may not be regarded as inventive either.

It is thus not possible to acknowledge an inventive step for the present set of claims.

The attention of the Applicant is also drawn to the fact that, even if he is able to demonstrate that the claimed processes provide an unexpected effect which could not be foreseen in view of the prior art, in order to acknowledge an inventive step, it must be credible that such an effect may be expected for the whole scope of the claims. With this regard, it should be noted that the lack of essential features (see point 5.1 here below) or the presence of unduly broad features such as "substituent" (see definition of R^5 - R^8 in the independent claims) or "optionally substituted hydrocarbon group" (see R^{13} in Claim 7), does not allow the recognition of an inventive step.

4.3 Industrial applicability (Art. 33(4) PCT)

It is acknowledged for all the claims.

5) Re Item VIII

The present set of claims presents several deficiencies in terms of clarity, contrary to Art. 6

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5.1 The high yield and, particularly, the high optical purity observed by the Applicant for the products resulting of the asymmetric hydrogenation claimed are a consequence of the use of a particular chiral catalyst. The chiral catalyst is thus considered to be an essential feature for carrying out the claimed process. Since the independent claims do not contain this feature they do not meet the requirement following from Article 6 PCT taken in combination with Rule 6.3(b) PCT that any independent claim must contain all the technical features essential to the definition of the invention.

5.2 The order and the dependency of the claims is misleading:

- Claims 10-13 depend upon independent claims 1-3, but have been placed after the dependent claims of Claim 7;

- Some independent claims comprise all the features of other independent claims and should be formulated as dependent claims (Rule 6.4 PCT). See for example independent claims 1, 2, and 18 which comprise all the features of Claim 15, or independent Claim 3, which is comprised within Claim 16.

5.3 Claim 10 relates to claims 1-3, but an acid of formula (5) is only mentioned in Claim 1 and not in claims 2 and 3.

5.4 Claim 7 and its counterpart in the description on pg. 68 are not clear when having a look at the examples of compounds of formula (12) mentioned on pg. 68-70. In the claim, the compound (12) has two stereogenic centres, whereas all the cited examples have only one.